09/403861 514 Rec'd 1/PTO 2 8 OCT 1999

SEQUENCE LISTING

(1) GENERAL INFORMATION:

- (i) APPLICANT:
 - (A) NAME: APPLIED RESEARCH SYSTEMS ARS HOLDING N.V.
 - (B) STREET: 14 JOHN B. GROSIRAWEG
 - (C) CITY: CURACAO
 - (E) COUNTRY: NETHERLANDS ANTILLES
 - (F) POSTAL CODE (ZIP): NONE
 - (G) TELEPHONE: 639300
 - (H) RELEFAX: 614129
- (ii) TITLE OF INVENTION: INTRACELLULAR MODULATORS OF APOPTOTIC CELL

DEATH PATHWAYS

- (iii) NUMBER OF SEQUENCES: 6
 - (iv COMPUTER READABLE FORM:
 - (A) MEDIUM TYPE: Rloppy disk
 - (B) COMPUTER: IBM AC compatible
 - (C) OPERATING SYSTEM PC-DOS/MS-DOS
 - (D) SOFTWARE: Patently Release #1.0, Version #1.30 (EPO)
- (2) INFORMATION FOR SEQ ID NO: 1:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1972 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 206..616
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

CTGGCTGCTG TGGAGTTTGT GACATACTAG GTGACACCCT TGGAGTCACT TCTCTTCAAC

TCCAGCTTAG AAGTGCCTGC CTGGCTCAGG GTCTGCACTG CAGCCTACTC CTTGCTTCAG 120

GGCCTGACTG CAACGCCAAA GCCTATCCTA TAGCGGCAGC GCCAGCAGCC ACTCAAACCA

GCCACAGCTC CCCGGCAACC GAACC ATG AAC ACC GAA ATG TAT CAG ACC CCC 232

Met Asn Thr Glu Met Tyr Gln Thr Pro 1 5 . --

ATG GAG GTG GCG GTC TAT CAG CTG CAC AAT TTC TCC ACC TCC TTC TTT 280

Met Glu Val Ala Val Tyr Gln Leu His Asn Phe Ser Thr Ser Phe Phe 10 15 20 25

TCT TCT CTG CTT GGA GGG GAT GTG GTT TCC GTT AAA CTG GAT AAC AGT 328

Ser Ser Leu Leu Gly Gly Asp Val Val Ser Val Lys Leu Asp Asn Ser 30 35 40

GCC TCC GGA GCC AGT GTG GTG GCC CTA GAC AAC AAG ATT GAG CAG GCC 376

Ala Ser Gly Ala Ser Val Val Ala Leu Asp Asn Lys Ile Glu Gln Ala
45 50 55

ATG GAC CTC GTG AAG AAC CAC CTG ATG TAC GCT GTG AGA GAG GAG GTG 424

Met Asp Leu Val Lys Asn His Leu Met Tyr Ala Val Arg Glu Glu Val 60 65 70

GAG GTC CTA AAG GAG CAG ATT CGT GAG CTG CTT GAG AAG AAC TCC CAG

Glu Val Leu Lys Glu Gln Ile Arg Glu Leu Leu Glu Lys Asn Ser Gln 75 80 85

CTG GAG CGC GAG AAC ACC CTC CTG AAG ACG CTG GCA AGC CCC GAG CAA 520

Leu Glu Arg Glu Asn Thr Leu Leu Lys Thr Leu Ala Ser Pro Glu Gln 90 95 100 105

CTG GAA AAG TTC CAG TCC CGG CTG AGC CCT GAA GAG CCA GCA CCT GAA 568

Leu Glu Lys Phe Gln Ser Arg Leu Ser Pro Glu Glu Pro Ala Pro Glu
110 115 120

GCC CCA GAA ACC CCG GAA ACC CCG GAA GCC CCT GGT GGT TCT GCG GTG

Ala Pro Glu Thr Pro Glu Thr Pro Glu Ala Pro Gly Gly Ser Ala Val 125 130 · 135

TAAGTGGCTC TGTCCTTAGG GTGGGCAGAG CCACATCTTG TTCTACCTAG TTCTTTCCAG 676

TTTGTTTTG GCTCCCAAG GGTCATCTCA TGTGGAGAAC TTTACACCTA ACATAGCTGG 736

TGCCAAGAGA TGTCCCAAGG ACATGCCCAT CTGGGTCCAC TCCAGTGACA GACCCCTGAC

AAAGAGCAGG TCTCTGGAGA CTAAGTTGCA TGGGGCCTAG TAACACCAAG CCAGTGAGCC 856

TGTCGTGTCA CCGGGCCCTG GGGGCTCCCA GGGCTGGGCA ACTTAGTTAC AGCTGACCAA 916

1.2

GGAGAAAGTA GTTTTGAGAT GTGATGCCAG TGTGCTCCAG AAAGTGTAAG GGGTCTGTTT 976

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TTCATTTCCA TGGACATCTT CCACAGCTTC ACCTGACAAT GACTGTTCCT ATGAAGAAGC 1036

CACTTGTGTT CTAAGCAGAA GCAACCTCTC TCTTCTTCCT CTGTCTTTTC CAGGCAGGGG 1096

CAGAGATGGG AGAGATTGAG CCAAATGAGC CTTCTGTTGG TTAATACTGT ATAATGCATG 1156

GCTTTGTGCA CAGCCCAGTG TGGGGTTACA GCTTTGGGAT GACTGCTTAT AAAGTTCTGT 1216

TTGGTTAGTA TTGGCATCGT TTTTCTATAT AGCCATAATG CGTATATATA CCCATAGGGC 1276

TAGATCTATA TCTTAGGGTA GTGATGTATA CATATACACA TACACCTACA TGTTGAAGGG 1336

CCTAACCAGC TTTGGGAGTA CTGACTGGTC TCTTATCTCT TAAAGCTAAG TTTTTGACTG 1396

TGCTAATTTA CCAAATTGAT CCAGTTTGTC CTTTAGATTA AATAAGACTC GATATGAGGG

AGGGAGGGA AGACCAGCCT CACAATGCGG CCACAGATGC CTTGCTGCTG CAGTCCTCCC 1516

TGATCTGTCC ACTGAAGACA TGAAGTCCTC TTTTGAATGC CAAACCCACC ATTCATTGGT 1576

GCTGACTACA TAGAATGGGG TTGAGAGAAG ATCAGTTTGG ACTTCACATT TTTGTTTTAA

1696

TTTTTCTTTT TTAAGTTCTT GTGGGGAAAC TTTGGGGTTA ATCAAAGGAT GTAGTCCTGT

GGTAGACCAG AGGAGTAACT AGTTTTGATC CTTTGGGGTG TGGAAAATGT ACCCAGGAAG 1816

CTTGTGTAAG GAGGTTCTGT GACAGTGAAC ACTTTCCACT TTCTGACACC TCATCCTGCT 1876

GTACGACTCC AGGATTTGGA TTTGGATTTT TCAAATGTAG CTTGAAATTT CAATAAACTT 1936

ТССТССТТТТ ТСТАААААТА ААААААААА ААААА 1972

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 137 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Met Asn Thr Glu Met Tyr Gln Thr Pro Met Glu Val Ala Val Tyr Gln

Leu His Asn Phe Ser Thr Ser Phe Phe Ser Ser Leu Leu Gly Gly Asp 25

Val Val Ser Val Lys Leu Asp Asn Ser Ala Ser Gly Ala Ser Val Val

Ala Leu Asp Asn Lys Ile Glu Gln Ala Met Asp Leu Val Lys Asn His

Leu Met Tyr Ala Val Arg Glu Glu Val Glu Val Leu Lys Glu Gln Ile

Arg Glu Leu Clu Lys Asn Ser Gln Leu Glu Arg Glu Asn Thr Leu 85

Leu Lys Thr Leu Ala Ser Pro Glu Gln Leu Glu Lys Phe Gln Ser Arg 100 105

Leu Ser Pro Glu Glu Pro Ala Pro Glu Ala Pro Glu Thr Pro Glu Thr 120 125

Pro Glu Ala Pro Gly Gly Ser Ala Val 130

- (2) INFORMATION FOR SEQ ID NO: 3:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: misc_feature
 - (B) LOCATION:1..20
 - (D) OTHER INFORMATION:/note= "PCR forward primer"
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

CCATCTGGGT CCACTCCAGT

20

- (2) INFORMATION FOR SEQ ID NO: 4:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 20 base pairs
 - (B) TYPE: nucl ic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: misc feature
 - (B) LOCATION:1..20
 - (D) OTHER INFORMATION:/note= "PCR reverse primer"
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

AGGACAGTGG GAGTGGCACC

- (2) INFORMATION FOR SEQ ID NO: 5:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1946 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (ix) FEATURE:
 - (A) NAME/KEY: CDS
 - (B) LOCATION: 241..642
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

AATTCGGGGG CCGTGGAGTT TGTGACATAC GAGGTGACAC CCCTCGAGTC ACTTCCCTTC

AACTCCAGCT GGAGCGCCTG CTTGGCTTTG GGTTCGTTCT GCAGCCTTCG CCCCGCTCCT 120

AGCCTCAGGG CCGGACTCCA GCGCAGAGCC CAGCCCAGCG CAGCCTGCCA GCAGCCACCC 180

AGCCGCCCAG CCGCCCAGCC CCGCACGAAA CCCGGCCAGA GCTTCCTAGC AGCCCGAGCC 240

ATG AAC ACC GAA ATG TAT CAG ACC CCC ATG GAG GTG GCG GTC TAC CAG 288 Met Asn Thr Glu Met Tyr Gln Thr Pro Met Glu Val Ala Val Tyr Gln CTG CAC AAT TTC TCC ATC TCC TTC TCT TCT CTG CTT GGA GGG GAT 336 Leu His Asn Phe Ser Ile Ser Phe Phe Ser Ser Leu Leu Gly Gly Asp 20 GTG GTT TCC GTT AAG CTG GAC AAC AGT GCC TCC GGA GCC AGC GTG GTG Val Val Ser Val Lys Leu Asp Asn Ser Ala Ser Gly Ala Ser Val Val 35 40 GCC ATA GAC AAC AAG ATC GAA CAG GCC ATG GAT CTG GTG AAG AAT CAT Ala Ile Asp Asn Lys Ile Glu Gln Ala Met Asp Leu Val Lys Asn His CTG ATG TAT GCT GTG AGA GAG GAG GTG GAG ATC CTG AAG GAG CAG ATC 480 Leu Met Tyr Ala Val Arg Glu Glu Val Glu Ile Leu Lys Glu Gln Ile 70 CGA GAG CTG GTG GAG AAG AAC TCC CAG CTA GAG CGT GAG AAC ACC CTG Arg Glu Leu Val Glu Lys Asn Ser Gln Leu Glu Arg Glu Asn Thr Leu 85 TTG AAG ACC CTG GCA AGC CCA GAG CAG CTG GAG AAG TTC CAG TCC TGT 576 Leu Lys Thr Leu Ala Ser Pro Glu Gln Leu Glu Lys Phe Gln Ser Cys CTG AGC CCT GAA GAG CCA GCT CCC GAA TCC CCA CAA GTG CCC GAG GCC 624 Leu Ser Pro Glu Glu Pro Ala Pro Glu Ser Pro Gln Val Pro Glu Ala 115 120

CCT GGT GGT TCT GCG GTG TAAGTGGCTC TGTCCTCAGG GTGGGCAGAG 672 Pro Gly Gly Ser Ala Val

CCACTAAACT TGTTTTACCT AGTTCTTTCC AGTTTGTTTT TGGCTCCCCA AGCATCATCT 732

CACGAGGAGA ACTITACACC TAGCACAGCT GGTGCCAAGA GATGTCCTAA GGACATGGCC 792

ACCTGGGTCC ACTCCAGCGA CAGACCCCTG ACAAGAGCAG GTCTCTGGAG GCTGAGTTGC 852

ATGGGGCCTA GTAACACCAA GCCAGTGAGC CTCTAATGCT ACTGCGCCCT GGGGGCTCCC 912

AGGGCCTGGG CAACTTAGCT GCAACTGGCA AAGGAGAAGG GTAGTTTGAG GTGTGACACC 972

-15446 <u>-21.</u>-

4 .. 4

AGTTTGCTCC AGAAAGTTTA AGGGGTCTGT TTCTCATCTC CATGGACATC TTCAACAGCT 1032

TCACCTGACA ACGACTGTTC CTATGAAGAA GCCACTTGTG TTTTAAGCAG AGGCAACCTC 1092

TCTCTTCTCC TCTGTTTCGT GAAGGCAGGG GACACAGATG GGAGAGATTG AGCCAAGTCA

GCCTTCTGTT GGTTAATATG GTATAATGCA TGGCTTTGTG CACAGCCCAG TGTGGGATTA 1212

CAGCTTTGGG ATGACCGCTT ACAAAGTTCT GTTTGGTTAG TATTGGCATA GTTTTTCTAT

ATAGCCATAA ATGCGTATAT ATACCCATAG GGCTAGATCT GTATCTTAGT GTAGCGATGT 1332

ATACATATAC ACATCCACCT ACATGTTGAA GGGCCTAACC AGCCTTGGGA GTATTGACTG

GTCCCTTACC TCTTATGGCT AAGTCTTTGA CTGTGTTCAT TTACCAAGTT GACCCAGTTT 1452

GTCTTTTAGG TTAAGTAAGA ACTCGAGAGT AAAGGCAAGG AGGGGGGCCA GCCTCTGAAT 1512

GCGGCCACGG ATGCCTTGCT GCTGCAACCC TTTCCCCAGC TGTCCACTGA AACGTGAAGT 1572

CCTGTTTTGA ATGCCAAACC CACCATTCAC TGGTGCTGAC TACATAGAAT GGGTTGAGAG 1632

TTGTGGAAAA CTTTCAAGTG AACAGAAGGA TGGTGTCCTA CTGTGGATGA GGGATGAACA 1752

AGGGGATGGC TTTGATCCAA TGGAGCCTGG GAGGTGTGCC CAGAAAGCTT GTCTGTAGCG 1812

GGTTTTGTGA GAGTGAACAC TTTCCACTTT TTGACACCTT ATCCTGATGT ATGGTTCCAG 1872

GATTTGGATT TTGATTTTCC AAATGTAGCT TGAAATTTCA ATAAACTTTG CTCTGTTTTT 1932

CTAAAAAATA AAAA 1946

(2) INFORMATION FOR SEQ ID NO: 6:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 134 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear



- (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

Met Asn Thr Glu Met Tyr Gln Thr Pro Met Glu Val Ala Val Tyr Gln 1 5 10 15

Leu His Asn Phe Ser Ile Ser Phe Phe Ser Ser Leu Leu Gly Gly Asp
20 25 30

Val Val Ser Val Lys Leu Asp Asn Ser Ala Ser Gly Ala Ser Val Val
35 40 45

Ala Ile Asp Asn Lys Ile Glu Gln Ala Met Asp Leu Val Lys Asn His 50 55 60

Leu Met Tyr Ala Val Arg Glu Glu Val Glu Ile Leu Lys Glu Gln Ile 65 70 75 80

Arg Glu Leu Val Glu Lys Asn Ser Gln Leu Glu Arg Glu Asn Thr Leu 85 90 95

Leu Lys Thr Leu Ala Ser Pro Glu Gln Leu Glu Lys Phe Gln Ser Cys 100 105 110

Leu Ser Pro Glu Glu Pro Ala Pro Glu Ser Pro Gln Val Pro Glu Ala 115 120 125

Pro Gly Gly Ser Ala Val